

both patients and health providers. A 1983 survey indicated that only 15 percent of women over 50 received annual mammograms, even though 80 percent of all breast cancer occurs in women over 50.

What are some of the barriers that keep women from putting into action what they know or what health providers know to be good practice? Fear probably is one of the major barriers, and there are many subsets of fears: radiation exposure, finding the disease, treatment, and death. These are often the specific reasons why women say that they will not participate in annual screening or do not specifically request mammography.

The amount of radiation needed to give clear views of the breast is less than 1 rd, much less than the amount delivered during early breast cancer screening trials. Should a malignant mass be discovered, the treatments are far less radical and far less mutilating to the woman, thus further relieving some of these fears.

There is a second major barrier, however, and that barrier is cost. Very few insurers will pay for breast cancer screening. For women who do not feel ill,

spending from \$20 to as much as \$200 can represent a great disincentive. We need to address this issue, because screening truly is cost effective.

We need to educate women on the need for mammography and give them the power of knowledge. Knowledge prodded women to go to their physicians to have the Pap smear done 20-25 years ago. The women of this country got the medical profession moving on that issue, and I think it will take a similar effort to get the medical profession moving on mammography. Survey data indicate that less than 15 percent of primary care physicians recommend annual mammography for their patients over the age of 50. We need education on both sides of the stethoscope on this issue.

The bottom line is that cancer is a very serious issue for women, but the good news is that many types of cancers can be prevented with reasonably simple changes in our lifestyle. Even with these changes, cancer is either going to touch our own person or touch someone we know in the immediate future, and we need to press on in our search for effective, less radical treatments for these persons.

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## Women's Health: Cancer

### Women and Lung Cancer

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#### Synopsis .....

*Lung cancer has now surpassed breast cancer as the leading cause of cancer deaths in American women. In 1986, 49,000 women were diagnosed as having lung cancer; only 16 percent of them will survive 5 years or more. Cigarette smoking is unquestionably the leading contributing factor.*

*Large numbers of women took up cigarette smoking during and after World War II. The grim aftermath*

*has taken 20 years to surface—between 1950 and 1985, lung cancer deaths in women increased 500 percent. Even worse, statistics to the end of this century will show no improvement because of the large number of teenage girls and young women now smoking.*

*Unfortunately, efforts at early diagnosis have usually been ineffective. By the time a chest X-ray reveals an abnormality, the patient is usually incurable. Surgery is currently the primary treatment, but is applicable only to those few women in whom the cancer has not spread and who are otherwise acceptable surgical candidates.*

*Scientists are studying chemotherapy and immunotherapy for treatment, as well as exploring the possible preventive effects of various vitamins and minerals. The results of these latter studies will not be available for many years.*

*It is estimated that people who stop smoking must allow 15 years for their risk to return to that of nonsmokers, but if every American woman gave up smoking today, by 2017 lung cancer in women might once again be a medical rarity.*

**L**UNG CANCER IS A GRAVE problem for today's American women. Figure 1 demonstrates the death rates for the male and female population, at eight cancer sites, for 1950-85. Offsetting—in fact more than offsetting—the decline in other cancers has been the soaring death rate from lung cancer. Between 1950 and 1985, lung cancer deaths in women increased more than 500 percent. By 2000, more American women than men will die of lung cancer.

For the first time in history, lung cancer has eclipsed breast cancer as the leading cause of cancer deaths among women. The 5-year survival rate for American women with breast cancer has been rising rapidly and is now 75 percent. By contrast, the survival rate for women with lung cancer is less than 20 percent. Breast cancer accounts for 26 percent of cancer incidence among women. But while lung cancer accounts for only 11 percent of cancer incidence among women, it kills more of us than any other cancer.

The American Cancer Society (1) estimates that in 1986 alone, 49,000 new cases of lung cancer were diagnosed among women in America and that 41,100 women with previously diagnosed cases died. Why has the death rate from lung cancer shown such an alarming increase, when the death rate from almost all the other cancers has remained the same or declined?

American women took up smoking in large numbers during and after World War II, much as American men became heavy smokers following World War I. Smoking by adult Americans age 20 and over was at a peak around 1965, when nearly 34 percent of women compared with 52 percent of men smoked (fig. 2). The percentage of men smoking has fallen sharply since—to 32.7 in 1985, a decline of 19.7 points. The percentage of women smoking has fallen much more slowly—to 28.3, a decline of only 5.9 points. Today in the U.S. almost as many women smoke as men, and many more men have quit smoking than women (2).

In every year since 1976, more girls than boys, age 12 to 18, have become smokers. In the 1985 survey of high school seniors by the National Institute on Drug Abuse, 31 percent of the girls said they had smoked in the previous month, compared with 28 percent of the boys (Institute data computed and summarized by Ted Kafalas, Associate, Epidemiology and Statistics Units, American Lung Association).

At the same time, differences in the way women used to smoke—starting later, smoking fewer cigarettes, not inhaling as much or as deeply as men—

have virtually disappeared (3), and lung cancer is rapidly becoming an equal-opportunity tragedy.

White women in their early 20s have the highest smoking rate—40 percent—of any group in the nation. Fewer young blacks of both sexes now smoke than whites, and fewer Hispanics smoke than either blacks or whites, although smoking among young Hispanic women is increasing (4).

There is a lag of roughly 20–25 years between the changes in the prevalence of cigarette smoking and the changes in the death rates from lung cancer. Therefore no decrease in the incidence of lung cancer (fig. 3) is expected before 2000. Some women have stopped, but many young women are starting. The rate of decline in smoking among women slowed significantly after 1978. More recently, smoking among women may have actually increased (5).

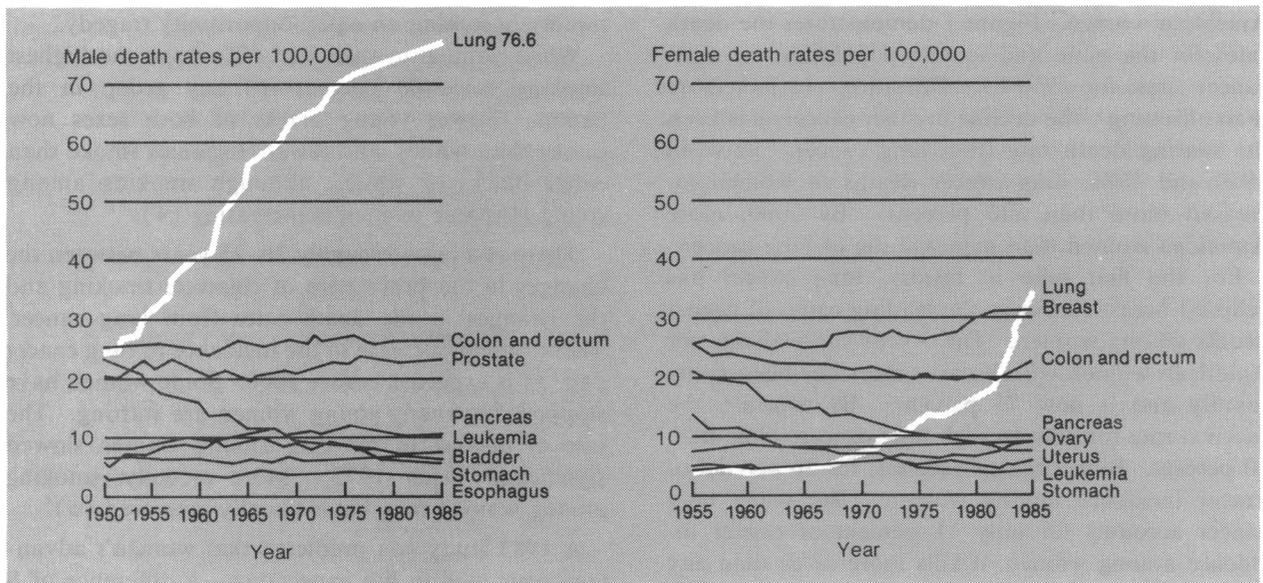
A 1983 study (6) predicted that women's advantage over men in life expectancy—a difference of 8 years according to 1980 census data—will soon vanish, largely because of smoking patterns among women. This study is controversial, but even its critics are likely to agree that women may lose at least half of those 8 years by the end of the century, again primarily because of smoking (personal communication, Estelle Ramey, Professor of Physiological Biology, Georgetown University Medical School, June 17, 1986).

I assume that most professionals are convinced that smoking does cause lung cancer and is by far the leading cause of lung cancer in the United States. If anyone remains unconvinced, I direct you to the 1982 report of the Surgeon General to the Congress titled "The Health Consequences of Smoking: Cancer." Perhaps I should add that there is no real controversy among medical professionals about this. Thousands of careful studies have documented the facts. I know of no major medical or health agency that questions them.

Other causes of lung cancer are, of course, known—asbestos, radioactivity, and industrial chemicals, separately and especially in combination with smoking. Still other causes are suspected—air pollution and so-called sidestream smoke—the smoke nonsmokers passively inhale in the presence of smokers. But the groups at risk from known causes other than smoking are comparatively small. And many authorities find the evidence for suspected causes, including passive smoking, to be inconclusive so far (7).

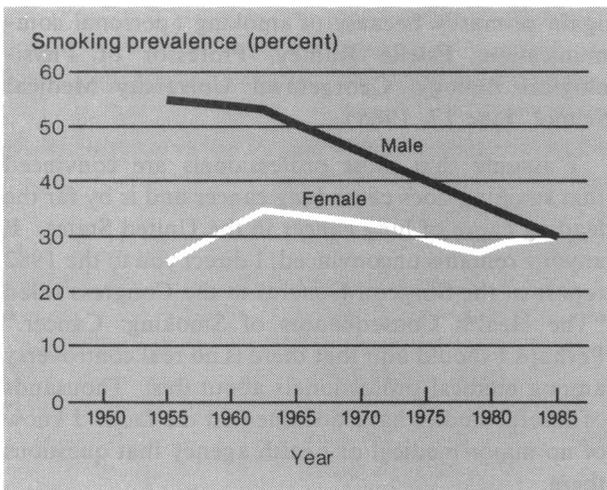
What we are left with then is a known cause of 75 percent of all lung cancer among women in this

Figure 1. Death rates: total population, eight cancer sites, 1950-85, age - adjusted to 1970



SOURCE: National Center for Health Statistics, U.S. Bureau of Census, and American Cancer Society.

Figure 2. Smoking rates: male and female 1950-85



SOURCE: National Center for Health Statistics, 1985.

country, and a high-risk group of 25-30 million women smokers.

Most people have heard that early detection is a key to surviving cancer. That is certainly true of many cancers that affect women. But I am sorry to report that, for the most part, the techniques of mass screening for early detection just do not work with lung cancer. Studies conducted by investigators at Johns Hopkins, Memorial Sloan-Kettering, and the Mayo Clinic cancer centers did not find that screening of men who had smoked heavily for a long time improved the survival rate of those who eventually

developed lung cancer. Infrequent, specialized screening for lung cancer is expensive and not nearly as effective as frequent doctor visits for general health checkups (8, 9). We presume the same would be true of women, although whether women with lung cancer have unique biological features remains to be seen.

In any case, one major problem is that the disease spreads so very quickly. A patient can have no detectable cancer, and in less than a year, a tumor can be detected that has already spread throughout the lung or to distant sites in the body.

Current diagnostic tools for lung cancer are not very useful. By the time we see a shadow on a chest X-ray or find cancer cells in the patient's sputum, it is usually too late (10, 11). New diagnostic approaches—some using genetic engineering techniques such as monoclonal antibodies and DNA probes—are being studied experimentally. But any actual tests that may come out of these approaches are years away from development and more years away from routine clinical use.

How then do physicians go about trying to save people with lung cancer today, and how successful are they?

More than 95 percent of lung cancers fall into four types. Three of these types, known collectively as nonsmall cell carcinomas, together account for about 80 percent of the lung cancers we see clinically (12).

The only proven cure for nonsmall cell lung cancers is surgery. Unfortunately, surgery is usually

indicated only when the tumor has not spread to other parts of the body. Also, the patient must qualify for surgery, in terms of her age and general condition, including respiratory and cardiac status. Only about 20 percent of nonsmall cell carcinoma patients will qualify. Worse, a third of those who do undergo surgery will show evidence of residual cancer, or cancer spreading to distant sites, within a month following their operations. Less than half of the 20 percent of nonsmall cell lung cancer patients who survive surgery will be alive 5 years following the procedure.

And what of the 80 percent with inoperable nonsmall cell lung cancer? Following diagnosis, their life expectancy is only 3–9 months. Half of all women in whom cancer has spread from the lung at the time of diagnosis are dead within 6 months of the time of first presentation.

So the success rate for surgery—currently the only proven cure for nonsmall cell lung cancer—is about 16 percent in women, a rate that has not improved by more than a few percentage points in decades.

What about radiation and chemotherapy? For most patients, they are little more than palliative. They make patients more comfortable, but they have not generally been shown to significantly lengthen life or improve chances for survival. Of course, there are occasional happy exceptions to this rule, but in general, we are not seeing marked increases in survival using these modalities.

As for the one in five patients with small cell carcinoma of the lung, surgery is usually not a modality of choice because by the time this disease can be detected in the lung, it has usually already spread to distant sites.

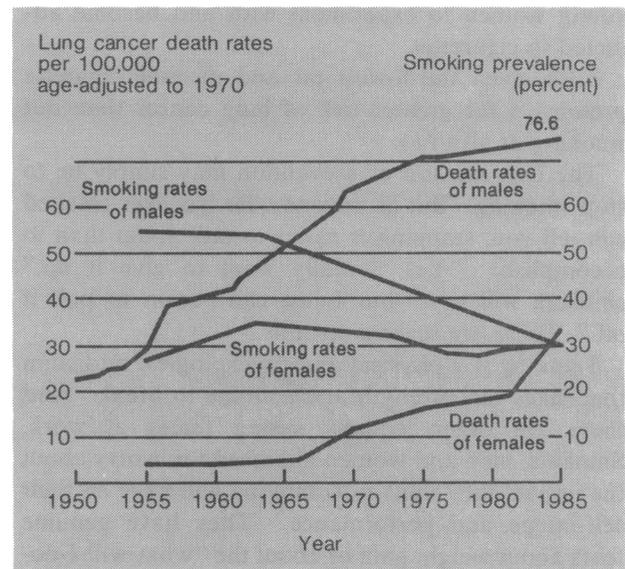
Chemotherapy and radiation are often effective in producing remissions of small cell carcinoma; and in a small percentage of the cases, the remissions are relatively long-term. In most cases, however, remission is temporary, and survival is only modestly prolonged.

Experimentally, there are combinations of different agents that kill cancer cells, with or without radiation therapy. In the clinic these agents have shown the ability to shrink both small cell and nonsmall cell tumors. There are, however, no studies as yet to show that long-term survival rates are affected in meaningful ways.

At this point in such a grim tale, it may be academic to point out that small cell carcinoma patients who stop smoking tend to survive longer than those who do not. And those who stopped smoking in the distant past survive longest of all.

Recently, there have been a number of reports concerning investigational use of a newer class of

**Figure 3. Lung cancer death rates and smoking rates: male and female, 1950–85**



SOURCE: Mortality data from WHO (1979, 1984); prevalence data from National Center for Health Statistics, 1985.

therapeutics called biological response modifiers. The compounds of this class that have received the most attention are interleukin-2 and interferon. They are interesting therapeutic options for some of the most common cancers, but they require much more investigation. Many centers are doing just that—using these drugs and evaluating different methodologies for administering them. But their clinical effects on lung cancer are not as yet fully determined.

Finally, a few words about lung cancer prevention.

Most of the evidence continues to suggest that the risk of lung cancer can be reduced by smoking cigarettes low in tar and nicotine. But the following caveats should be kept in mind:

First, evidence is mounting that many individuals who switch to low tar and nicotine cigarettes modify their smoking techniques so as to maintain the desired level of nicotine, the habituating agent. This has been documented by blood-level testing (11).

Second, cigarette smoke contains many dangerous chemicals, not just tar and nicotine. Many conventional filter cigarettes deliver more carbon monoxide, for example, than nonfilter cigarettes. Hydrogen cyanide is yet another constituent of cigarette smoke (3).

Third, it has not been established that lower tar and nicotine cigarettes are any less dangerous to an unborn fetus, to women with elevated cholesterol or blood pressure, to women working with industrial chemicals, or to anyone who already has a smoking-related illness.

Fourth, it has not yet been determined whether low tar and nicotine cigarettes make it easier for young women to experiment with and become addicted to cigarettes.

Fifth, even the lowest tar and nicotine cigarette presents a far greater risk of lung cancer than not smoking at all (11).

The best method of prevention may simply be to stop smoking. But as anyone who has ever smoked can tell you, stopping is easier to talk about than to accomplish. "Yes, I really want to give it up," smokers will say, "but I just can't seem to pull it off." There are reasons for this.

Smoking is a physical and psychological addiction that takes real strength and courage to break. And there are other, equally strong forces at work. Smokers, men and women alike, tend to worry about the impact they think not smoking will have on their self-image and performance. They have genuine fears about weight gain or about the "what-will-I-do-with-my-hands?" syndrome in professional and social situations. This is not an issue to be taken lightly. Quitting is hard to do.

Even for those who succeed in stopping smoking, the prognosis is not all that good. By the latest estimate, it takes about 15 years for someone who has been a heavy smoker to lower her risk of lung cancer to that of a nonsmoker.

On the other hand, there may be good news concerning efforts at cancer prevention. Some evidence in the scientific literature suggests that some vitamins and minerals may exert preventive effects against lung cancer and other cancers associated with smoking, as well as cancers in general. Several important studies are currently being conducted under the auspices of the National Cancer Institute in collaboration with academia and industry to evaluate the use of naturally occurring forms of vitamins, such as beta-carotene, in populations at high risk because of smoking or other known related factors, such as exposure to asbestos. But the best method of prevention, of course, is never to start smoking.

Smoking causes 75 percent of all cases of lung cancer in women, and lung cancer is now the leading cancer killer of women in the United States. What's more, there's little hope that the situation will improve before the turn of the century. And it may not improve much then unless American women start now to quit at the same rate as American men.

The earlier you start to smoke, the more you smoke, and the longer you keep it up, the more likely you are to get lung cancer. If you have been smoking for some time, there is nothing you can take, nothing you can do, to lower quickly your elevated risk of developing lung cancer. Even 10 years after quitting,

your risk may still be 5 times that of a nonsmoker (13). But that is still better than not quitting and perpetuating your risk at 16 times that of a nonsmoker.

If you do get lung cancer, chances are it will not be diagnosed in time for you to be a candidate for life-saving surgery. Even if the diagnosis does come in time and you have an operation, your chances of long-term survival are less than 50-50. The treatments now available, while of at least temporary benefit, will probably not lengthen your life significantly, and your chances of living for any length of time are minimal at best.

Now, let us be honest about instant medical miracles. For the next decade at least and perhaps longer, rising rates of lung cancer are going to follow yesteryear's increases in smoking among women just as surely as night follows day.

Still, the only absolute certainty in all of this is that if every American woman were to give up smoking today, lung cancer among us would be rare—a medical oddity—by 2017. Women are showing no signs of suddenly giving up cigarette roulette. So we are just going to have to live—or rather die—with an epidemic of lung cancer until we get a medical breakthrough or come to our senses.

## References .....

1. American Cancer Society: 1986 Cancer facts and figures.
2. Department of Health and Human Services, Public Health Service: Pre-publication data from the National Health Interview Survey, 1985, NCHS, CDC.
3. Department of Health and Human Services, Public Health Service: The health consequences of smoking for women: A report of the Surgeon General, Introduction and summary. U.S. Government Printing Office, Washington, DC, 1980, pp. 3-42.
4. Patrick Remington, Centers for Disease Control, quoted by Susan Okie: Smoking now worst threat to women's health. Washington Post, November 11, 1985, p. A1, col. 2.
5. "Drug abuse by high school seniors, class of 1986." In *NIDA Capsule*, NIDA, ADAMHA, PHS, DHHS, March 1987.
6. Miller, D.H., and Gerstein, D.: The life expectancy of nonsmoking men and women. *Public Health Rep* 98: 343-349, July-August 1983.
7. Weiss, S.T.: Passive smoking and lung cancer: what is the risk? *Am Rev Respir Dis* 133: 1-3, January, 1986.
8. Berlin, Nathaniel I., et al: Early lung cancer detection. *Am Rev Respir Dis* 130: 545-570 (1984).
9. Geddes, D.M., et al: Lung Cancer: Future prospects. *Recent Results Cancer Res* 92: 118-127 (1984).
10. Minna, J.D., et al: Cancer of the lung. In *Cancer principles and practice of oncology*, edited by V.T. Devita, 1985, pp. 507-597.
11. Loeb, L.A., et al: Smoking and lung cancer: An overview. *Cancer Res* 44: 5940-5958, December 1984.
12. Rosenow, E.C., and Carr, D.T.: Bronchogenic carcinoma. *Cancer* 29: 233-245 (1979).
13. Doll, P., and Peto, R.: Mortality in relation to smoking: 20 years' observations on male British doctors. *Br Med J* 2: 1525-1527 (1976).